



DTIC FILE COPY

2

AD-A217 813

Laboratory Note No. 89-77

Plasma Dextran Concentrations in Trauma
Patients Administered HSD.

C.Wade, B. Ryan, J. Summary, M. Dubick, M. Vassar, C.
and Perry, J. Holcroft

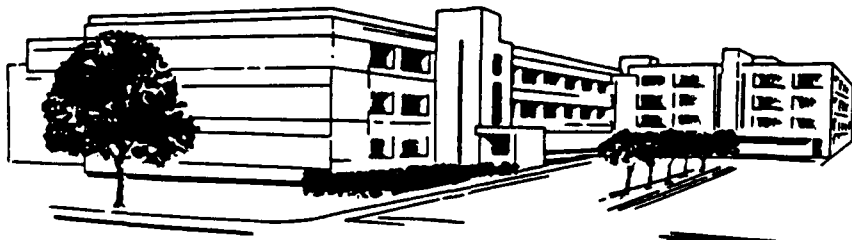
DIVISION MILITARY TRAUMA RESEARCH

NOVEMBER 1989

DISTRIBUTION STATEMENT A

Approved for public release;
Distribution Unlimited

DTIC
ELECTE
FEB 06 1990
S E D



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

90 02 06 200

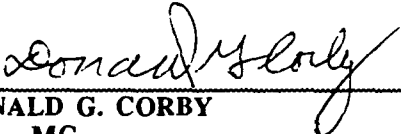
Reproduction of this document in whole or in part is prohibited except with the permission of the Commander, Letterman Army Institute of Research, Presidio of San Francisco, California 94129-6800. However, the Defense Technical Information Center is authorized to reproduce the document for United States Government purposes.

Destroy this report when it is no longer needed. Do not return to the originator.

Citation of trade names in this report does not constitute an official endorsement or approval of the use of such items.

This Document has been approved for public release and sale; its distribution is unlimited.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. (AR 360-5)


DONALD G. CORBY
COL, MC
Commanding

28 Nov 89
(date)

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION Unclassified			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release, Distribution is Unlimited.		
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
4. PERFORMING ORGANIZATION REPORT NUMBER(S) Lab Notes 89-77			7a. NAME OF MONITORING ORGANIZATION U. S. Army Medical Research and Development Command		
6a. NAME OF PERFORMING ORGANIZATION Division of Military Trauma		6b. OFFICE SYMBOL (If applicable) SGRD-ULT-M	7b. ADDRESS (City, State, and ZIP Code) Ft. Detrick Frederick, MD 21701-5012		
6c. ADDRESS (City, State, and ZIP Code) Letterman Army Institute of Research Presidio of San Francisco, CA 94129-6800			9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER		
8a. NAME OF FUNDING / SPONSORING ORGANIZATION		8b. OFFICE SYMBOL (If applicable)	10. SOURCE OF FUNDING NUMBERS		
8c. ADDRESS (City, State, and ZIP Code)		PROGRAM ELEMENT NO. 63807A	PROJECT NO. D836	TASK NO. AX	WORK UNIT ACCESSION NO. 087
11. TITLE (Include Security Classification) (U) Plasma dextran concentrations in trauma patients administered HSD.					
12. PERSONAL AUTHOR(S) C Wade, B Ryan, J Summary, M Dubick, M Vassar, C Perry, J Holcroft.					
13a. TYPE OF REPORT Lab Notes		13b. TIME COVERED FROM _____ TO _____		14. DATE OF REPORT (Year, Month, Day) Oct 1989	
15. PAGE COUNT 10					
16. SUPPLEMENTARY NOTATION					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP	(U) Hypertonic saline/Dextran, plasma concentrations, dextran, sodium, potassium. (S)		
19. ABSTRACT (Continue on reverse if necessary and identify by block number) To determine the plasma concentrations of dextran, sodium and potassium, blood samples were obtained from 13 trauma patients treated with hypertonic saline/dextran (HSD). The dose of HSD was 250 ml, or 3.6±0.2 ml/kg. Blood samples were taken 27±5 min after the administration of HSD. Plasma levels of sodium were increased, (155±1 mEq/l) while potassium concentrations (4.0±0.5 mEq/l) were within normal range. Plasma dextran concentrations (244±27 mg/dl), were significantly less than expected, thereby suggesting either a rapid rate of clearance, association with TCA-precipitable materials, or a larger volume of distribution. These data will provide the basis for future in vitro and in vivo studies as to the efficacy of HSD, and indicate that HSD administration does not result in dangerous alterations in serum electrolyte or dextran concentrations. (S)					
20. DISTRIBUTION / AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION Unclassified		
22a. NAME OF RESPONSIBLE INDIVIDUAL COL Donald G. Corby, MC, Commanding			22b. TELEPHONE (Include Area Code) 561-3600		22c. OFFICE SYMBOL SGRD-ULZ

ABSTRACT

To determine the plasma concentrations of dextran, sodium and potassium, blood samples were obtained from 13 trauma patients treated with hypertonic saline/dextran (HSD). The dose of HSD was 250 ml or 3.6 ± 0.2 ml/kg. Blood samples were taken 27 ± 5 min after the administration of HSD. Plasma levels of sodium were increased (155 ± 1 mEq/l), while potassium concentrations (4.0 ± 0.5 mEq/l) were within normal range. Plasma dextran concentrations (244 ± 27 mg/dl) were significantly less than expected, thereby suggesting either a rapid rate of clearance, association with TCA-precipitable materials, or a larger volume of distribution. These data will provide the basis for future in vitro and in vivo studies as to the efficacy of HSD, and indicate that HSD administration does not result in dangerous alterations in serum electrolyte or dextran concentrations.

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	



Plasma dextran concentrations in trauma patients administered hypertonic saline/dextran -- Wade et al.

INTRODUCTION

A hypertonic/oncotic solution has recently been introduced for the resuscitation of trauma patients hypotensive due to hemorrhage (1-3). This solution consists of 7.5% NaCl in 6% Dextran-70 and is known as HSD. Concern has been raised as to the degree of hypernatremia and hypokalemia induced by the administration of HSD (1,4,5), as well as possible adverse effects of dextran administration (6-8). The present study investigates the levels of sodium, potassium and dextran in trauma patients who received HSD, and will provide a basis for future in vitro and in vivo studies.

METHODS

Blood samples were obtained from 13 patients who were treated with 250 ml of HSD (Pharmacia AB, Uppsala Sweden) as a part of a larger prospective, randomized, double-blinded, placebo-controlled study evaluating the efficacy of the solution (1,2). This study was approved by the Human Subjects Review Committee at the University of California at Davis. The patients enrolled in the present study were randomly selected from the larger test population.

The patients were transported to the hospital by a Life Flight helicopter system, and all had significant hypotension upon entry into the study (systolic blood pressure <90). The HSD solution was administered intravenously, usually via percutaneously inserted catheters, over a period of 2-5 min en route to the hospital. All other aspects of the patients' care were those normally used. Additional fluid (Lactated Ringer's) was administered as clinically indicated. The time of administration of the HSD was noted and all additional fluid volumes given were recorded.

Upon arrival in the emergency room, a venous blood sample was taken for the measurement of hematocrit and plasma total protein, glucose, total carbohydrate, sodium and potassium levels. Dextran concentration was calculated as the difference between plasma total carbohydrate and glucose concentration (9).

In the text mean values and SEM values are given.

RESULTS

The mean weight of the patients was 72.3 ± 3.9 kg (Table I). The patients received 1108 ± 1399 ml of fluid prior to the administration of HSD. As each patient received 250 ml of HSD, the delivered dose was 3.6 ± 0.2 ml/kg. The time from the initiation of the dose of HSD to the collection of the blood sample was 26.7 ± 4.5 min. Over this period of time the patients received 845 ± 279 ml of additional fluids. Only one of the 13 patients died.

Upon arrival in the emergency room, the patients were significantly hemodiluted as indicated by low hematocrit ($27.4 \pm 2.8\%$) and total plasma protein levels (3.3 ± 0.4 g/dl) compared to normals (34-50% and 6.0-8.0 g/dl respectively) (Table II). Plasma concentration of sodium was increased (155 ± 1 mEq/l) compared to normal values, 135-145 mEq/l. One patient was clinically hypernatremic with plasma sodium levels greater than 160 mEq/l. Plasma potassium levels (4.0 ± 0.1 mEq/l) tended to be normal (3.5-5.0 mEq/l), with two patients being hypokalemic with concentrations less than 3.5 mEq/l. Plasma dextran concentrations ranged from 114.8 to 457.9 mg/dl with a mean of 243.9 ± 26.9 mg/dl.

DISCUSSION and CONCLUSIONS

The observed hemodilution upon admission to the emergency room reflects not only the infusion of crystalloid fluids, but also the transcapillary influx of fluid into the vascular space following hemorrhage and facilitation of this process by HSD administration (1-3,10,11). These processes result in a decrease in hematocrit and total plasma protein levels by simple dilution.

It has been suggested that hypernatremia and hypokalemia are of major concern in the administration of the HSD resuscitation solution (1,4,5). While clinical hypernatremia was observed in one of our patients, this has been reported to resolve within a short period of time (2). Hypokalemia was noted in two, 15%, of the patients. In one of the patients the incidence was borderline low with a potassium level of 3.4 mEq/l. In the other patient the potassium concentration was 2.9 mEq/l, and did not reflect a

significant hemodilution. No adverse effects associated with hypernatremia or hypokalemia were observed.

The circulating level of dextran, 244 mg/dl, was significantly less than expected. In a 70 Kg euvoletic man the plasma volume is assumed to be on the order of 2250 ml. If 250 ml of HSD which has 6% dextran (15 g) were added to this volume, the final dextran concentration would be 600 mg/dl. Due to the hemodilution effect of dextran, this concentration could actually achieve 500 mg/dl. As the trauma patients in the present study experienced significant hemorrhage, consequently reducing their plasma volume, the concentration of dextran should have been greater than 500 mg/dl. The low plasma levels observed in the present study suggest a rapid clearance sequestration or binding of dextran, a larger volume of distribution or hemodilution. The clearance of dextran has a half life on the order of six hours (9,12). As the blood samples were obtained within half an hour of HSD administration, the clearance of dextran would be minimal.

Fibrinogen is one of the plasma proteins cited to increase in response to tissue injury and other inducers of metabolic traumatic stress (13). Numerous studies have reported that dextrans may react with fibrinogen (7,14). If this conjugate is formed in vivo following HSD infusion, any dextran bound would be removed by TCA precipitation, rendering this dextran unavailable for assay. It is unknown whether such an effect could account, in part, for the lower than expected dextran concentrations observed in this study. Nevertheless, to avoid this possibility, we recommend performing dextran assays on serum samples. The dextran used in the present study had a mean molecular weight of 70k. Thus there was a quantity of lower molecular weight dextran which could have leaked out of the vascular space and been distributed into the interstitial fluid accounting for the increase in distribution volume. The decrease in dextran concentration could also be the product of hemodilution due to the large quantities of fluids administered following HSD. While hematocrit values agreed closely with the volume of fluid infused ($r=0.60$, $n=13$, $P<0.05$) a relationship to dextran levels was not present ($r=0.22$, $n=13$, $p=0.46$). Factors other than hemodilution due to the administration of additional fluids must further lower dextran levels. The lower

4 -- Wade et al.

levels of plasma dextran observed in trauma patients could be the product of a variety of factors and warrants further study to possibly improve the efficacy of HSD.

REFERENCES

1. Holcroft JW, Vassar MJ, Perry CA, Gannaway WL, Kramer GC. Use of a 7.5% NaCl/6% Dextran-70 solution in the resuscitation of injured patients in the emergency room. *Perspect Shock Res* 1989;331-338.
2. Holcroft JW, Vassar MJ, Turner JE, Derlet RW, Kramer GC. 3% NaCl and 7.5%/Dextran 70 in the resuscitation of severely injured patients. *Ann Surg* 1987;206:279-288.
3. Maningas PA, Mattox KL, Pepe PE, Jones RL, Feliciano DV, Burch JM. Hypertonic saline-dextran solutions for the prehospital management of traumatic hypotension. *Am J Surg* 1989;157:528-534.
4. Gunther RA, English PT, Holcroft JW, Kramer GC. Hypokalemia follows both hypertonic and isotonic resuscitation of hemorrhage. *FASEB Journal* A549, 1982.
5. Mattar JA. Hypertonic and hyperoncotic solutions in patients. *Editorial Crit Care Med* 1989;17(3):297.
6. Ring J, Messmer K. Incidence and severity of anaphylactoid reaction of colloid volume substitutes. *Lancet* I 1977;466-469.
7. Gruber UF. *Blood Replacement*. Berlin: Springer-Verlag, 1969.
8. Bartholomew JR, Bell WR, Kickter T, Williams GM. A prospective study of the effect of dextran administration of compatibility testing. *Transfusion* 1986;26:431-433.
9. Dubick MA, Summary JJ, Ryan BA, Wade CE. Dextran in plasma and urine following administration of 6% Dextran-70/7.5% NaCl to hemorrhaged and euvoletic conscious swine. *Circ Shock* (in press).
10. Kramer GC, Perron PR, Linsey C, et al. Small-volume resuscitation with hypertonic saline dextran solution. *Surgery* 1986;100:239-246.

-- Wade et al.

11. Wade CE, Hannon JP, Bossone CA, et al. Resuscitation of conscious pigs following hemorrhage: comparative efficacy of small-volume resuscitation with normal saline, 7.5% NaCl, 6% Dextran 70, and 7.5% in 6% Dextran 70. Circ Shock (in press).
12. Arturson G, Wallenius G. The intravascular persistence of dextran of different molecular sizes in normal humans. Scand J Clin Lab Invest 1964;16:76-80.
13. Bull JP, Ricketts C, Squire JR, et al. Interaction of dextran and fibrinogen. Lancet 1949;i:131.
14. Fleck A. Acute phase response: Implications for nutrition and recovery. Nutrition 1989;4(2): 109-117.

Table I: Subject Characteristics

<u>Subject #</u>	<u>Body Wt (kg)</u>	<u>HSD Dose¹ (ml/kg)</u>	<u>Volume Infusion Prior to HSD (ml)</u>
1	70	3.6	0
2	80	3.1	0
3	60	4.2	0
4	70	3.6	400
5	85	2.9	2,300
6	100	2.5	100
7	55	4.6	200
8	58	4.3	1,200
9	80	3.1	3,800
10	80	3.1	4,000
11	72	3.5	1,000
12	50	5.0	500
13	<u>80</u>	<u>3.1</u>	<u>900</u>
x	72.3	3.6	1,108
SD	13.9	0.7	1,399
SEM	3.9	0.2	388

¹Each patient received 250 ml of HSD²This includes the 250 ml of HSD

<u>Subject #</u>	<u>Total Volume Infused² at Time of Sample (ml)</u>	<u>Time of Blood Sample Min Post HSD</u>	<u>Patient Outcome</u>
1	350	11	Lived
2	250	6	Lived
3	950	38	Lived
4	1270	25	Lived
5	2550	45	Lived
6	350	14	Lived
7	950	34	Lived
8	5270	63	Died
9	4250	20	Lived
10	5000	18	Lived
11	1800	10	Lived
12	950	28	Lived
13	<u>1450</u>	<u>35</u>	Lived
x	1,953	26.7	
SD	1,773	16.2	
SEM	492	4.5	

Table II: Blood Values

<u>Subj. #</u>	<u>Hematocrit (%)</u>	<u>Total Pro- tein (g/dl)</u>	<u>Sodium (mEq/l)</u>	<u>Potassium (mEq/l)</u>	<u>Glucose (mg/dl)</u>
1	40.9	6.2	150	3.4	22.4
2	32.5	4.4	159	3.9	155.9
3	32.0	3.0	157	2.9	183.6
4	21.8	3.2	154	4.2	350.5
5	17.3	1.9	157	4.5	199.7
6	38.5	5.2	151	3.7	0.8
7	34.9	3.2	151	3.6	101.9
8	7.7	1.1	157	4.1	193.6
9	28.6	3.7	152	4.1	29.5
10	27.6	3.4	154	4.3	74.6
11	12.2	1.6	154	4.5	221.6
12	29.4	4.2	165	4.6	85.0
13	<u>32.8</u>	<u>2.4</u>	<u>158</u>	<u>4.4</u>	<u>73.4</u>
x	27.4	3.3	155.3	4.0	130.2
SD	10.0	1.4	4.1	0.5	98.7
SEM	2.8	0.4	1.1	0.1	27.4

<u>Subject #</u>	<u>Total Carbohydrate (mg/dl)</u>	<u>Dextran (mg/dl)</u>
1	137.2	114.8
2	429.9	274.0
3	485.6	302.0
4	635.0	284.5
5	334.5	134.8
6	287.7	286.9
7	384.8	282.9
8	326.1	132.5
9	340.2	310.7
10	328.0	253.4
11	376.8	155.2
12	542.9	457.9
13	<u>254.3</u>	<u>180.9</u>
x	374.1	243.9
SD	128.2	96.8
SEM	35.6	26.9

OFFICIAL DISTRIBUTION LIST

Commander
US Army Medical Research
& Development Command
ATTN: SGRD-RMS/Mrs. Madigan
Fort Detrick, MD 21701-5012

Defense Technical Information Center
ATTN: DTIC/DDAB (2 copies)
Cameron Station
Alexandria, VA 22304-6145

Office of Under Secretary of Defense
Research and Engineering
ATTN: R&AT (E&LS), Room 3D129
The Pentagon
Washington, DC 20301-3080

DASG-AAFJML
Army/Air Force Joint Medical Library
Offices of the Surgeons General
5109 Leesburg Pike, Room 670
Falls Church, VA 22041-3258

HQ DA (DASG-ZXA)
WASH DC 20310-2300

Commandant
Academy of Health Sciences
US Army
ATTN: HSHA-CDM
Fort Sam Houston, TX 78234-6100

Uniformed Services University of
Health Sciences
Office of Grants Management
4301 Jones Bridge Road
Bethesda, MD 20814-4799

US Army Research Office
ATTN: Chemical and Biological
Sciences Division
PO Box 12211
Research Triangle Park, NC 27709-2211

Director
ATTN: SGRD-UWZ-L
Walter Reed Army Institute of Research
Washington, DC. 20307-5100

Commander
US Army Medical Research Institute
of Infectious Diseases
ATTN: SGRD-ULZ-A
Fort Detrick, MD 21701-5011

Commander
US Army Medical Bioengineering Research and
Development Laboratory
ATTN: SGRD-UBG-M
Fort Detrick, Bldg 568
Frederick, MD 21701-5010

Commander
US Army Medical Bioengineering
Research & Development Laboratory
ATTN: Library
Fort Detrick, Bldg 568
Frederick, MD 21701-5010

Commander
US Army Research Institute
of Environmental Medicine
ATTN: SGRD-UE-RSA
Kansas Street
Natick, MA 01760-5007

Commander
US Army Research Institute of
Surgical Research
Fort Sam Houston, TX 78234-6200

Commander
US Army Research Institute of
Chemical Defense
ATTN: SGRD-UV-AJ
Aberdeen Proving Ground, MD 21010-5425

Commander
US Army Aeromedical Research
Laboratory
Fort Rucker, AL 36362-5000

AIR FORCE Office of Scientific
Research (NL)
Building 410, Room A217
Bolling Air Force Base, DC 20332-6448

USAF School of Aerospace Medicine
Document Section
USAFSAM/TSKD
Brooks Air Force Base, TX 78235-5301

Head, Biological Sciences Division
OFFICE OF NAVAL RESEARCH
800 North Quincy Street
Arlington, VA 22217-5000

Commander
Naval Medical Command-02
Department of the Navy
Washington, DC 20372-5120